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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/942,098	08/28/2001	Lance E. Steward	17451 (BOT)	6185

23601 7590 10/06/2003  
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EXAMINER

MINNIFIELD, NITA M

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 10/06/2003

10

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/942,098

Applicant(s)

STEWART ET AL.

Examiner

N. M. Minnifield

Art Unit

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 14 July 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-8 and 45-67 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-8 and 45-67 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892) 3 sheets
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.

- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

## **DETAILED ACTION**

1. Applicant's election without traverse of Group I, claims 1-8 and 45-67, in Paper No. 9 is acknowledged. The Examiner acknowledges that claim 67 should be group with Group I as set forth above.

2. Applicants' amendment filed July 14, 2003 is acknowledged and has been entered. Claims 9-44 and 78-95 have been canceled. Claims 1-8 and 45-67 are now pending in the present application.

3. The use of trademarks has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

4. Claims 1-8 and 45-67 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are vague and

indefinite in the recitation of “under the appropriate conditions”; what specifically are these conditions? The metes and bounds of these conditions do not appear to be set forth or defined in the specification. Claims 54-59 are indefinite because it contains the use of trademarks (see claims), absent sufficiently detailed descriptive generic terminology and the products denoted by trademark names are subject to change. Such trademarks, absent generic terminology, should not be used in the claims. Although trademarks accompanied by generic terminology may be used in the claims, the use of the generic terminology alone is preferred since redundancy and the use of parentheticals in the claims should be avoided. Claims 45-49 are vague and indefinite in the recitation of “can be cleaved”; it is not clear if cleavage will or will not occur. Claim 5 recites the limitation “human SNAP-25” in line 2. There is insufficient antecedent basis for this limitation in the claim. Claims 64-67 recite the limitation “said acceptor fluorophore”. Claim 1 does not recite a “acceptor fluorophore”. There is insufficient antecedent basis for this limitation in the claim.

5. Claims 45-50 are objected to because of the following informalities: claims 45-50 depend from canceled claims 9, 14, 21, 26, 31, 36 and 40; claims 45 recites “nanomoles” and it should be “nanomole”. Appropriate correction is required.

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759

F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1-8 and 45-67 provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6, 11, 13-15 and 31-38 of copending Application No. 10/261161. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications claim and disclose a substrate composition comprising clostridial toxin recognition sequence (i.e. botulinum toxin or BoNT/A), donor fluorophore and acceptor.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1-8 and 45-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holskin et al 1995 (Analytical Biochemistry, 226:148-155) taken with Ekong et al 1997 (Microbiology, 143:3337-3347).

Holskin et al teaches substrates that comprise a donor fluorophore, acceptor fluorophore and a protease having a specific cleavage site (abstract). Holskin et

al teaches the specific fluorophores of EDANS and DABCYL (abstract). Holskin et al teaches that donor and acceptor pair EDANS and DABCYL, respectively, have excellent spectral overlap properties resulting in efficient energy transfer and that strategies incorporating this donor/acceptor pair have been successfully applied to fluorescence-based assays for HIV protease, renin as well as others (p. 149, col. 1; p. 152). The prior art teaches the claimed invention except for the specific use of clostridial toxins or BoNT/A. However, Ekong et al teaches the use of SNAP-25 as an effective substrate for clostridial BoNT/A endopeptidase activity in vitro. A segment of SNAP-25 spans the toxin cleavage site and thus this action can be used in various assays (abstract). Clostridial neurotoxin, BoNT/A cleaves SNAP-25 at Gln<sub>197</sub>-Arg<sub>198</sub> and this action of BoNT/A provides a basis for the development of a functional assay for the toxin utilizing its endopeptidase activity. A substrate (the BoNT/A) and a means of monitoring the cleavage of the substrate are needed (p. 3338). It would have been obvious to a person of ordinary skill in the art at the time the invention was made to combine the teachings of Holskin et al with Ekong et al to prepare a substrate complex as taught in Holskin et al, a fluorescence-based assay, which has the donor and acceptor fluorophores and the substrate with the substrate being a clostridial toxin. Although Holskin et al does not specifically teach BoNT/A the prior art does teach this concept with several other proteins and substrates to assay for potency of therapeutic compositions and to monitor potential inhibitors. Therefore, the use of SNAP-25 and BoNT/A in a similar substrate complex would have been obvious to a person of ordinary skill in the art with the reasonable expectation of success since it had been proven successful in other substrate compositions. The claimed

invention is prima facie obvious in view of the prior art teachings as a whole, absent any unexpected evidence to the contrary.

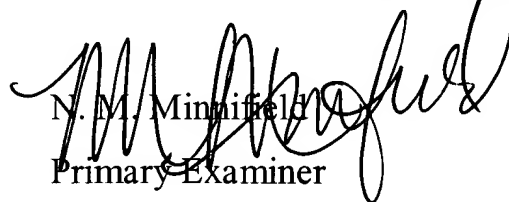
12. No claims are allowed.

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 703-305-3394. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 703-308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



N. M. Minnifield  
Primary Examiner

Art Unit 1645

NMM

September 28, 2003